

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k112416

B. Purpose for Submission:

New Device

C. Measurand:

Creatine phosphokinase (CPK) / Creatine kinase (CK)

D. Type of Test:

Quantitative enzymatic assay

E. Applicant:

Vital Diagnostics (Manufacturing) Pty Ltd.

F. Proprietary and Established Names:

Vital Diagnostics CPK Reagent

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
CGS	Class II	862.1215 Creatine Phosphokinase/Creatine kinase or isoenzymes test system.	Clinical Chemistry (75)

H. Intended Use:

- Intended use(s):
Please see indication use below.
- Indication(s) for use:
Vital Diagnostics CPK Reagent is a device intended to measure the activity of the enzyme creatine phosphokinase in plasma and serum. Measurements of creatine phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial

infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.

3. Special conditions for use statement(s):
For prescription Use.
4. Special instrument requirements:
Roche Hitachi 911

I. Device Description:

The Vital Diagnostics CPK Reagent is a dual reagent system containing reagents for use on the Roche Hitachi 911 analyzer.

Reagent 1 (R1) contains 123 mmol/L imidazole buffer, 2.46 mmol/L EDTA, 12.3 mmol/L Mg^{2+} , 2.46 mmol/L ADP, 6.14 mmol/L AMP, μ mol/L diadenosine pentaphosphate, 2.46 mmol/L NADP, 24.6 mmol/L N-acetylcysteine, ≥ 2.2 KU/L HL (yeast), ≥ 1.5 KU/L G6P-DH (*E. coli*) stabilizers and preservatives.

Reagent 2 (R2) contains 20 mmol/L 3-(cyclohexylamino)-2-hydroxy-1-propanesulfonic acid and buffer, 120 mmol/L glucose, 2.46 mmol/L EDTA, 184 mmol/L creatine phosphate and preservative.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Roche Creatine Kinase (CK) Liquid Reagent
2. Predicate 510(k) number(s):
k921661
3. Comparison with predicate:

Attribute	Vital Diagnostics CPK Reagent (Candidate Device)	Creatine Kinase (CK) Liquid (Predicate - k921661)
Indication for use / Intended for Use	It is intended to measure the activity of the enzyme creatine phosphokinase in plasma and serum. Measurements of creatine phosphokinase and its isoenzymes are used in the diagnosis and treatment of myocardial infarction and muscle diseases such as progressive, Duchenne-type muscular dystrophy.	Same
Sample	serum and plasma	Same
Reagent type	Two part liquid	Same
Reaction Type/Test Methodology	Enzymatic Rate	Same
Linearity range	8 – 2300 U/L	3 – 2300 U/L
Storage Temperature after opening (onboard)	10°C	2-8°C
Onboard Stability Claim	28 days	Same
Shelf life	15 months @ 2-8°C	12 months

K. Standard/Guidance Document Referenced (if applicable):

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline- Second Edition (CLSI EP5-A2)

Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline (CLSI EP6-A)

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline- Second Edition (CLSI EP9-A2)

Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline (CLSI EP17-A)

L. Test Principle:

The test consists of a series of oxidation/reduction reaction in which the rate of increase in absorbance at 340nm as NADPH is formed is measured. The increase in absorbance is proportional to the activity of CPK in the sample.

M. Performance Characteristics (if/when applicable):**1. Analytical performance:****a. *Precision/Reproducibility:***

Within-Run and Total precision evaluations were determined following CLSI EP5-A2. Three levels of serum control material were tested on one Roche Hitachi 911 analyzer. Two runs per day, two replicates of each level per run for 20 days.

Within Run	Level 1	Level 2	Level 3
No. of data points	80	80	80
Mean (U/L)	47.9	341.9	633.5
SD (U/L)	2.1	6.1	7.3
CV (%)	4.5	1.8	1.2

Total	Level 1	Level 2	Level 3
No. of data points	80	80	80
Mean (U/L)	47.9	341.9	633.5
SD (U/L)	2.4	7.6	10.7
CV (%)	5.0	2.2	1.7

b. *Linearity/assay reportable range:*

Linearity studies were carried out using dilutions of a stock standard. Ten concentrations were prepared by diluting the serum based standard with saline. All samples were measured in duplicate. The sample range tested was 4 to 2355 U/L.

Claimed Measuring Range	Intercept	Slope	95% CI Slope	p Value for Polynomial fit analysis
8 to 2300 U/L	7.8	0.997	0.990 to 1.004	0.072

Based on the linearity data, the measuring range claimed from 8-2300 U/L was supported.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Traceability

This method does not require calibration but utilizes an enzyme calibration factor to calculate Creatine Kinase (CK) enzyme activity. The enzyme calibration factor was determined using a commercial Calibrator for Automated Systems which has a CK set-point traceable to the International Federation of clinical chemistry and laboratory medicine reference method for CK at 37°C.

d. Detection limit:

Limit of Detection studies were carried out using one blank and one low serum samples. Both samples were assayed multiple times on one instrument, in two separate runs. Detection Limits (LoB and LoD) were performed using 60 blank and 60 low standard samples as per the recommendations of CLSI EP17A protocol. LoB and LoD were calculated to be: LoB claim: 4 U/L and LoD claim is 8 U/L.

e. Analytical specificity:

Interference studies were performed by spiking normal sera at two CPK concentrations with individual interferents at a range of concentrations. The sera, both spiked and unspiked, were assayed for CPK ($n \geq 3$ replicates) and the mean result calculated. Interference was deemed NOT to be significant by the sponsor if for a spiked sample the mean recovery was within 90 to 110 % of that obtained with the unspiked serum. The results reported were obtained on a Hitachi 911 analyzer using fresh Vital CPK Reagent.

Interferent Claim

Hemoglobin	No interference up to 1000 mg/dL*
Lipaemia	No interference up to 500 mg/dL
Bilirubin	No interference up to 60 mg/dL

*Labeling states moderate to severely hemolyzed specimens are not considered suitable because enzymes and intermediates (AK, ATP and G-6-P) liberated from erythrocytes may cause erroneous results.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Studies were carried out according to CLSI EP09-A.

Roche CK was used as the predicate method, using Roche recommended applications and procedures on a Roche Hitachi 911 analyzer and calibrating with Roche Calibrator for Automated Systems (CFAS). Sixty seven serum samples were assayed in parallel by both the test and predicate methods and the results compared by regular linear regression and Deming regression. The range tested was 8 to 2120 U/L. Some samples were altered.

The comparison by regular linear regression resulted in a slope of 0.948 (95%CI = 0.942 to 0.955), an intercept of 3.636 (95%CI = 0.199 to 7.073), correlation coefficient of $R^2 = 0.9992$, and a std. error of 17.774.

The comparison by Deming regression resulted in a slope of 0.950 (95%CI = 0.942 to 0.957), an intercept of 2.823 (95%CI = -1.810 to 7.455), correlation coefficient of $R^2 = 0.9992$, and a std. error of 20.2.

b. *Matrix comparison:*

Parallel samples from 46 individuals were collected (range 8 to 2021 U/L) as serum and anti-coagulated (Lithium Heparin) plasma. Paired samples for each individual were tested by both the candidate and the predicate device. Results were compared by regular linear regression and Deming regression according to CLSI EP9.

The comparison by regular linear regression resulted in a slope of 0.988 (95%CI = 0.981 to 0.995), an intercept of 5.626 (95%CI = 2.523 to 8.728), correlation coefficient of $R^2 = 0.9994$ and a std. error of 13.4.

The comparison by Deming regression resulted in a slope of 0.989 (95%CI = 0.982 to 0.996), an intercept of 5.512 (95%CI = 2.409 to 8.615), correlation coefficient of $R^2 = 0.9994$, and a std. error of 13.4.

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable.

b. *Clinical specificity:*

Not Applicable.

c. *Other clinical supportive data (when a. and b. are not applicable):*

Not Applicable

4. Clinical cut-off:
Not Applicable.
5. Expected values/Reference range:
The expected values are 34- 171 U/L¹.

1. Burtis CA, Ashwood ER, eds. Tietz textbook of clinical chemistry and molecular diagnostics. 4th Ed. Philadelphia PA: W.B. Saunders Company; 2006.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.